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Epidemiology of Patients Presenting with Dyspnea to Emergency Departments in Europe and Asia-Pacific region

RUNNING HEAD "Dyspnea at the ED"

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CONFLICTS OF INTEREST:

None declared.

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ABSTRACT

Objective:

The primary objective of this study was to describe the epidemiology and management of dyspneic patients presenting to emergency departments (EDs) in an international patient population. Our secondary objective was to compare the EURODEM and AANZDEM patient populations.

Methods: An observational prospective cohort study was performed in Europe and Asia-Pacific region. The study included consecutive patients presenting to EDs with dyspnea as the main complaint. Data was collected on demographics, co-morbidities, chronic treatment, clinical signs and investigations, treatment in the ED, diagnosis, and disposition from ED.

Results: A total of 5569 patients were included in the study. The most common ED diagnoses were lower respiratory tract infection (LRTI) (24.9%), heart failure (HF) (17.3%), chronic obstructive pulmonary disease (COPD) exacerbation (15.8%) and asthma (10.5%) in the overall population. There were more LRTI, HF and COPD exacerbations in the EURODEM population whereas Asthma was more frequent in the AANZDEM population. Intensive care unit (ICU) admission rates were 5.5%. ED mortality was 0.6%. Overall in-hospital mortality was 5.0%. In hospital mortality rates were 8.7% for LRTI , 7.6% for HF and 5.6% for COPD patients.

Conclusions: Dyspnea as a symptom in the ED has substantial ward and ICU admission rates. A variety of causes of dyspnea was observed in this study, with chronic diseases accounting for a major proportion.

KEYWORDS:

Dyspnea, emergency department, management, epidemiology, outcome

INTRODUCTION

Dyspnea is one of the main complaints of patients presenting to the emergency department (ED)[1]. In the United States, dyspnea accounts for 3 to 4 million ED visits annually[2,3] representing up to 50% of patients admitted to acute tertiary care hospitals[4,5]. In the Asia-Pacific region it accounts for 5% of all ED presentations[6]. Diagnosis and treatment of the underlying cause of dyspnea is the most efficient approach to improve symptoms. However, establishing accurate diagnoses for ED dyspneic patients remains challenging. Sensitivity of the clinical signs associated with this symptom is low, especially in an aging population and the variety of underlying diseases[7-10].

Little is known about the etiology, epidemiology and outcome of dyspneic patients presenting to the EDs worldwide. Understanding patient characteristics, the range of diagnoses, outcome and regional differences could help improve emergency care of affected patients.

Therefore, the primary objective of this study was to describe the epidemiology and management of dyspnea patients presenting to emergency departments (EDs) in an international patient population. Our secondary objective was to compare the EURODEM and AANZDEM patient populations.

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METHODS

Study design

This is a combination of two international, multicenter, prospective, observational, cohort studies. They were designed to evaluate the epidemiology and outcomes of patients presenting to the ED with dyspnea as the main complaint. The EURODEM study (*NCT02060799*) was conducted in 66 European EDs in Belgium (n=3), Finland (n=5), France (n=5), Germany (n=5), Italy (n=1), the Netherlands (n=16), Romania (n=7), Spain (n=1), Turkey (n=7) and United Kingdom (n=16). The AANZDEM study was conducted in 46 Asia-Pacific centers in Australia (n=33), New Zealand (n=4), Singapore (n=3), Hong Kong (n=4) and Malaysia (n=2). The study sample was generated with consecutive patients attending EDs during three study periods of 72 hours throughout one year. [6,11] European centers recruited patients during three consecutive days in February, May and October 2014, whereas inclusion dates for Australasian centers were in May, August and November. These dates were chosen to represent different seasons (autumn, winter and spring) in each region.

Patient population

Consecutive adult patients (18 years and older) presenting to the ED with acute dyspnea as the main symptom were included. The study was performed in accordance with the Declaration of Helsinki. Ethics committee approvals were obtained for all sites according to local requirements. If requested by the local ethics committee, patient consent for data collection was obtained.

Study variables

A specifically designed data collection form was developed by each steering committee (see Annex). Data collected included patient characteristics, co-morbidities, mode of arrival, usual

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medications, prehospital treatment as documented in ED clinical records, initial assessment (clinical assessment and vital signs), investigations performed (laboratory tests, electrocardiogram (ECG), imaging, etc.) and results, treatment in the ED, ED diagnosis (diagnosis after ED management), outcome after the ED including disposition, in-hospital outcome and final hospital diagnosis.

Outcomes of interest

The primary outcome of interest was the proportion of patients in each etiologic category of dyspnea, their management at the ED and in-hospital mortality. Our secondary objective was to compare the characteristics of European patients' (EURODEM study) to those of the Asia-Pacific region (AANZDEM study).

Statistical analysis

Results are presented as frequencies for qualitative variables and as mean (stdev) or medians with interquartile range for quantitative variables depending on distribution. The chi-square test was used to compare categories. The means of continuous variables were compared using the t-test (parametric) and the Wilcoxon test (nonparametric). Statistical significance was defined as $p < 0.05$. Statistical analysis was performed using SAS version 9.1 software (SAS Institute, Cary, NC, USA).

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RESULTS

Patient characteristics

A total of 5569 patients were included in the study. Patient characteristics are summarized in **table 1**. Median age of patients was 68 [51-80] years and nearly half of the cohort were male. In approximately half of all cases, emergency physicians considered the cause of dyspnea to be of pulmonary origin and in a quarter of cases the cause of dyspnea was considered to be of cardiac origin. The most common ED diagnoses were lower respiratory tract infection (LRTI) (24.9%), heart failure (17.3%), COPD exacerbation (15.8%) and asthma (10.5%). A substantial proportion of patients had other diagnoses than the ones listed.

The most frequent comorbidities were hypertension (46.9%), chronic obstructive pulmonary disease (COPD) (27.3%) and diabetes mellitus (23.0%). About half of patients presented to the ED by ambulance (49.3%).

Vital and clinical signs at admission are summarized in **table 2**. Of all patients, 4.3% presented with confusion, 28.1% had signs of peripheral edema and 77.9% had abnormalities at lung auscultation (rales, wheezing or ronchi). A proportion of patients presented with vital signs indicating a severe clinical condition: 10% had tachycardia (heart rate > 120 bpm/min), 13.6% had oxygen saturation below 90%, and 4.7% were hypotensive (systolic blood pressure < 100 mmHg).

Management and outcomes

Initial ED investigations are summarized in supplementary table 1. Supplementary Table 2 describes treatment modalities at the EDs. The most commonly used medical therapies were inhaled β2 agonists (35.6%), antibiotics (29.5%) and corticosteroids (23.7%).

Nearly two-thirds of the total study population were hospitalized after initial care at the ED. 5.5% of patients were admitted to the ICU and 0.6% died in the ED. Overall in-hospital

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mortality rate was 5.0%. In hospital mortality rates were 8.7% for LRTI, 7.6% for HF and 5.6% for COPD patients.

Regional differences

The EURODEM patient population was slightly older than the AANZDEM cohort, median age 69 [53-80] years vs. 67 [49-80] years, (p=0.01).

There were more LRTI, HF and COPD exacerbations in the EURODEM population whereas Asthma was more frequent in the AANZDEM population. EURODEM patients more often had a prior history of chronic heart failure, COPD, smoking and cognitive dysfunction.

A higher ward admission rate was observed in Asia-Pacific than in Europe (60.6% vs. 56.4%, p<0.01). However, the proportions of ED deaths (0.9% vs. 0.4%, p=0.03) and intensive care unit (ICU) admissions (8.4% vs. 3.4%, p<0.001) were higher in the EURODEM cohort. In hospital mortality was also significantly higher in EURODEM compared to the AANZDEM cohort (6.5% vs. 4.1%, p<0.001).

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DISCUSSION

This study describes the epidemiology and contemporaneous management of dyspnea in EDs in Europe and Asia-Pacific region. Our results confirm that patients presenting to the ED with dyspnea represent a diverse and complex group. The most common causes of dyspnea in the ED were LRTI, decompensated (or acute) heart failure, COPD exacerbations and asthma. The high proportion of 'other' diagnoses (including unknown) is somewhat surprising and a salient reminder that the causes of dyspnea are legion and that careful clinical assessment is required to differentiate between them. Importantly, our study demonstrates that dyspneic patients require immediate and high-quality care as the majority is admitted to hospital with not infrequent admissions to intensive care units[13,14]. This study emphasizes the challenges that ED physicians face while striving for accurate and prompt diagnosis and treatment.

The most common diagnoses of dyspnea at the ED were LRTI, heart failure, COPD exacerbation and asthma. Our results seem to be in accordance with previous studies: Bilben and colleagues observed that COPD, cardiac failure, and pneumonia accounted for symptoms in 29, 24 and 22% of dyspneic ED patients respectively[12]. Even though lung and heart diseases were the main causes of dyspnea in the ED, it seems that a pulmonary origin (infection, COPD and asthma combined) was twice as common than a cardiac origin of dyspnea. This finding might help guide emergency physicians in cases where it is difficult to differentiate between both causes.

The results of our study illustrate a diverse clinical profile of dyspneic patients at the ED in Europe compared to Asia-Pacific region. Dyspneic ED patients were mostly elderly, with 25% of patients being older than 80 years. There is no gender predilection for this symptom. As expected in an elderly population, patients presented with many comorbidities. These concomitant illnesses can make it difficult to ascertain the specific diagnosis based on clinical

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presentation in patients with dyspnea, and patients may have mixed disease contributing to the dyspnea.

In both cohorts a significant proportion of patients presented with clinical signs suggesting a critical condition: tachycardia (10%), tachypnea (11%), low oxygen saturation (14%) and hypotension (5%). Therefore, high hospital admission rates as well as ICU admission and in-hospital death were in line with disease severity.

Our study confirms that dyspnea is a high risk condition for in-hospital mortality. We report in-hospital mortality of 5.0% which is similar to previously reported mortality rates in acute heart failure[15], community acquired pneumonia[16] and COPD exacerbations[17].

Our study shows that there were more ED deaths and ICU admissions in the EURODEM cohort. In-hospital mortality was also higher in Europe. This could be due to the increased frailty of EURODEM patients, suggested by their older age, higher rates of cognitive dysfunction and pre-existing chronic conditions. Differences in primary care provision might also account for these disparities.

Our study has an important clinical impact for emergency physicians. It shows that acute management of dyspneic patients can be improved. It also highlights the need for an appropriate discharge analysis, as dyspnea at the ED was associated with a risk of ICU admission as well as in-hospital death. Our study also demonstrated that in the majority of cases, acute dyspnea was caused by an exacerbation of a pre-existing chronic condition. This emphasizes the importance of chronic disease management in primary care and outpatient settings, as preventing exacerbations of chronic heart failure or COPD could possibly reduce the burden of frequent ED visits and recurrent hospitalizations.

Future research should be directed at understanding the source of the heterogeneities in patient characteristics as well as management differences between regions. Subsequent analyses are planned on subpopulations of the EURODEM and AANZDEM studies by

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etiology of dyspnea. Future projects will include a more precise description of the four most frequent diseases causing dyspnea. We are also aiming to identify differences between the current real-life management of these diseases and treatment guidelines.

LIMITATIONS

Our study has several limitations. Since this was a multi-center registry, it should be taken into account that some centers recorded data differently than others. There was also no central committee for the establishment of final diagnosis or the appropriateness of administered treatment. One of the limitations of this work is that in the EURODEM study, it was allowed to include more than one diagnosis per patient whereas in the AANZDEM study only the principal diagnosis was collected. However, study sample is large and presents all comers suggesting generalization of findings. Moreover, local data collectors had the possibility to contact the coordinating center if they had any queries regarding data collection therefore minimizing bias. There is also a certain amount of missing data that may have influenced results.

CONCLUSION

In summary, Dyspneic patients represent a heterogeneous group with a wide variety of clinical profiles and etiologies of dyspnea in both hemispheres. The population affected by this symptom is mostly elderly and have high rates of comorbidities. Exacerbations of chronic diseases such as heart failure and COPD account for a large proportion of dyspneic patients. Dyspnea at the ED was associated with a high rate of ward admission as well as sub-optimal short-term outcome. Our study also showed that the EURODEM patients were more ill than AANZDEM patients, presenting with more comorbidities and higher rates of ICU admission and hospital death.

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Table 1: Patient characteristics

	Total	AANZDEM	EURODEM	p value	OR [95% CI]
N (%)	5569	3044 (54.7%)	2525 (45.3%)		
Age (years), (median [Q1-Q3])	68 [51-80] missing data n= 25	67 [49-80]	69 [53-80]	0.01	
Male (N, %)	2719 (49.0%) missing data n=21	1495 (49.2%)	1224 (48.8%)	NS	1.02 [0.91-1.13]
ED diagnoses (N, %)					
Lower respiratory tract infection	1389 (24.9%)	616 (20.2%)	773 (30.6%)	p<0.001	0.58 [0.51-0.65]
Heart failure	962 (17.3%)	455 (14.9%)	507 (20.1%)	p<0.001	0.63 [0.55-0.73]
COPD exacerbation	882 (15.8%)	415 (13.6%)	467 (18.5%)	p<0.001	0.70 [0.60-0.81]
Asthma	584 (10.5%)	387 (12.7%)	197 (7.8%)	p<0.001	1.52 [1.27-1.82]
Other	2022 (36.3%)	1171 (38.5%)	851 (33.7%)	p<0.001	1.24 [1.10-1.38]
Co-morbidities (N, %)					
Chronic heart failure	1102 (20.5%) missing data n=196	522 (17.2%)	580 (24.7%)	p<0.001	0.63 [0.55-0.73]
Diabetes mellitus	1246 (23.0%) missing data n=149	697 (23.0%)	549 (22.9%)	NS	1.01 [0.89-1.14]
Hypertension	2541 (46.9%) missing data n=152	1405 (46.4%)	1136 (47.6%)	NS	0.95 [0.85-1.06]
Atrial fibrillation / flutter	873 (16.1%) missing data n=157	468 (15.5%)	405 (17.0%)	NS	0.90 [0.77-1.04]
COPD	1477 (27.3%) missing data n=164	721 (23.9%)	756 (31.7%)	p<0.001	0.67 [0.60-0.76]
Smoker	935 (17.9%) missing data n=336	389 (12.9%)	546 (24.7%)	0.001	0.45 [0.39-0.52]
Asthma	1117 (20.6%) missing data n=143	685 (22.6%)	432 (18.0%)	0.03	1.33 [1.16-1.53]

COPD: chronic obstructive pulmonary disease.

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Table 2: Clinical signs at admission

	Total	AANZDEM	EURODEM	p value	OR [95% CI]
Vital signs at admission					
SBP (mmHg), (median [Q1-Q3])	135 [120-154] missing data n=138	136 [120-154]	135 [120-153]	0.21	
SBP<100mmHg (N, %)	257 (4.7%)	141 (4.7%)	116 (4.7%)	0.01	1.01 [0.78-1.31]
Heart rate (bpm), (median [Q1-Q3])	90 [77-106] missing data n=115	92 [78-106]	89 [77-105]	p<0.001	
heart rate >120 bpm (N, %)	547 (10.0%)	323 (10.8%)	224 (9.1%)	0.04	1.21 [1.01-1.45]
Respiratory rate (cycles/min), (median [Q1-Q3])	21 [18-26] missing data n=566	22 [18-26]	20 [18-26]	p<0.001	
Respiratory rate >30 cycles/min (N, %)	550 (11.0%)	334 (11.3%)	216 (10.5%)	NS	1.09 [0.90-1.31]
SpO2 <90% (N, %)	685 (13.9%) missing data n=652	308 (12.3%)	377 (15.7%)	NS	0.75 [0.64-0.89]
Temperature <35 or >38° C (N, %)	477 (9.2%) missing data n=392	282 (9.7%)	195 (8.6%)	NS	1.14 [0.94-1.39]
Clinical signs at admission (N, %)					
Confusion	237 (4.3%) missing data n=96	75 (2.5%)	162 (6.6%)	p<0.001	0.36 [0.27-0.48]
Rales	1953 (37.4%) missing data n=346	912 (31.5%)	1041 (44.7%)	p<0.001	0.57 [0.51-0.64]
Wheezing	1220 (24.0%) missing data n=496	590 (20.4%)	630 (28.9%)	p<0.001	0.63 [0.55-0.72]
Rhonchi	826 (16.5%) missing data n=571	280 (9.7%)	546 (25.9%)	p<0.001	0.31 [0.26-0.36]

SBP: systolic blood pressure, SpO_2: saturation level of oxygen in hemoglobin determined by pulse oximetry.

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Supplementary table 1: diagnostic investigations at the ED

Laboratory parameters at admission	Total	AANZDEM	EuroDEM	Mean difference [95%CI]	p value
Creatinine (µmol/L, median, Q1-Q3)	82 (65-110) performed n=3645 (65.5%)	83 (66-112)	79 (63-104)	NA	p<0.001
Sodium (mmol/L, mean, std)	137.85 (4.56) performed n=4587 (82.4%)	137.72 (4.34)	137.99 (4.78)	0.28 [0.01-0.54]	0.04
Potassium (mmol/L, mean, std)	4.20 (0.62) performed n=4469 (80.2%)	4.17 (0.61)	4.24 (0.64)	0.07 [0.03-0.11]	p<0.001
CRP (mg/dL, median, Q1-Q3)	18 (5-70) performed n=2418 (43.4%)	30 (9-115)	13 (4-47)	NA	p<0.001
$PaCO_2$ (mmHg, mean, std)	41.36 (16.85) performed n=1306 (23.5%)	46.62 (20.48)	38.20 (13.29)	8.42 [6.58-10.25]	p<0.001
White cell count (median, Q1-Q3)	9.2 (7-12) performed n=3781 (67.9%)	9.1 (7-11.8)	9.25 (7-12.2)	0.64 [0.16-1.12]	0.01
pH (mean, std)	7.39 (0.10) performed n=2302 (41.3%)	7.37 (0.11)	7.40 (0.09)	0.03 [0.02-0.04]	p<0.001
D-dimer elevated (N,%)	301 (55.4%) performed n=543	56 (52.8%)	245 (56.1%)	NA	

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	(9.8%)				
Haemoglobin (g/l, mean, std)	12.72 (2.61) performed n=4434 (79.6%)	12.58 (2.87)	12.72 (2.61)	0.31 [0.16-0.47]	p<0.001

CRP: C-reactive protein.

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Supplementary table 2: Management at the ED and outcomes

	Total	AANZDEM	EuroDEM	p value	OR [95% CI]
Treatment in the ED (N, %)					
NIV	289 (5.2%) missing data n=201	145 (4.8%)	144 (5.7%)	NS	0.80 [0.63-1.03]
IV diuretics	1010 (18.6%) missing data n=134	468 (15.5%)	542 (22.5%)	p<0.001	0.63 [0.55-0.72]
Oral diuretics	117 (3.4%) missing data n=2146	84 (2.8%)	33 (8.2%)	p<0.001	0.32 [0.21-0.50]
IV vasodilators	200 (3.7%) missing data n=149	50 (1.7%)	150 (6.3%)	p<0.001	0.25 [0.18-0.35]
Oral/sublingual vasodilators	246 (7.8%) missing data n=2434	193 (6.4%)	53 (47.7%)	p<0.001	0.07 [0.05-0.11]
IV inotropes/ vasopressors	52 (1.0%) missing data n=169	24 (0.8%)	28 (1.2%)	NS	0.67 [0.37-1.20]
Antibiotics	1607 (29.5%) missing data n=123	938 (31.0%)	669 (27.6%)	0.01	1.18 [1.04-1.33]
Inhaled Beta-2 agonists	1941 (35.6%) missing data n=110	1019 (33.7%)	922 (37.9%)	0.02	0.83 [0.74-0.93]
Corticosteroids (IV or oral)	1295 (23.7%) missing data n=116	762 (25.2%)	533 (22.0%)	0.01	1.19 [1.05-1.36]
Discharge from the ED (N, %)					
Home	2003 (36.8%) missing data n=129	1081 (35.6%)	922 (38.4%)	0.03	0.88 [0.79-0.99]

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Ward	3118 (57.3%) missing data n=129	1843 (60.6%)	1275 (53.1%)	p<0.001	1.36 [1.22-1.52]
Intensive care unit	283 (5.2%) missing data n=129	103 (3.4%)	180 (7.5%)	p<0.001	0.43 [0.33-0.56]
Death in ED	36 (0.7%) missing data n=129	13 (0.4%)	23 (1.0%)	0.016	0.44 [0.21-0.92]
In hospital outcome (N, %)					
Mortality	254 (5.0%) missing data n=535	125 (4.1%)	129 (6.5%)	p<0.05	0.62 [0.48-0.80]

NIV: non-invasive ventilation, IV: intravenous.

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